REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

I. Introduction

Claims 39 and 50 have been amended by incorporating the limitations from claims 41 and 51, respectively. Claims 41 and 51 have been cancelled. New claims 61-66 have been added. Support for the new claims may be found on pages 12-14 of the specification and in Figures 14A, 14B and 15. No new matter was added.

II. The Rejections Should Be Withdrawn

A. Rejections Over Li

Claims 39, 43-50 and 53-59 are rejected under §102(b) as being anticipated by Li (J. Vac. Sci. Technol. 1994). Claims 39 and 50 have been amended by incorporating the limitations from claims 41 and 51, respectively. Thus, this rejection has been rendered moot.

B. Rejections Over Li and Thaysen

Claims 41, 42, 51 and 62 are rejected under §103(a) as being unpatentable over Li in view of Thaysen (J. Phys. D. 2002). This rejection is respectfully traversed.

1. No Motivation To Combine

There is no motivation to combine Li and Thaysen, since the cantilever of Li is not suitable for detection of biological analyte. The cantilever of Li is a 4 mm wide silicon beam which is clamped at one end (see page 813, col. 2, paragraph 2 of Li). The 4 mm size of the beam is clearly too large to be useful for detection of biological analyte. Since biological analyte is generally several orders of magnitude smaller than the 4 mm beam of Li, the

binding of biological analyte to the 4 mm beam of Li would not cause sufficient beam deflection to cause a sufficient signal to result in the detection of the biological analyte.

For example, the size of the cantilever of Thaysen, which is alleged to be useful for bio-sensor applications, is 100 by 200 by 7.6 microns, as shown in Table 1 of Thaysen. Thus, one of ordinary skill in the art would not be motivated to use the beam of Li for detection of biological analyte, since the beam of Li is too large to obtain suitable results for bio-sensing.

Furthermore, independent claims 39 and 50 recite a biofunctionalized cantilever. As defined on page 10, lines 20-21, the term "biofunctionalized" means that the cantilever surface is coated with another material which is adapted to selectively bind to a biological analyte.

In contrast, Thaysen does not expressly teach biofunctionalization of the cantilever surface. Thaysen merely makes general statements about bio-molecular interactions and molecular immobilization on the cantilever surface (see page 2698, page 2702 and page 2703, col. 2, paragraph 1 of Thaysen). However, Thaysen does not expressly teach that the cantilever surfaces are coated with another material which is adapted to selectively bind to a biological analyte, as recited in claims 39 and 50. Specifically, the cantilever of Thaysen was tested by bending the cantilever by a micromanipulator, not by selective binding of a biological analyte, as explained on page 2701, section 5.1 (titled "Sensitivity") of Thaysen.

Thus, there is motivation to combine Li and Thaysen to form a biofunctionalized surface of the beam of Li.

2. Claims 43 and 53

Claims 43 and 53 recite a cantilever made of an inorganic material. In contrast, the key feature of the device of Thaysen is the use of an organic polymer cantilever material (SU-8 polymer). Thaysen teaches that the SU-8 cantilever is easier and cheaper to fabricate than the silicon cantilever (page 2698, col. 1, and page 2703, section 6 of Thaysen). Thus, Thaysen explicitly teaches to substitute a silicon cantilever with an organic polymer cantilever.

As noted in MPEP § 2141.02(VI), "a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)." Thus, when the Thaysen reference is considered as a whole, it teaches to substitute a silicon cantilever with a polymer cantilever.

Therefore, if there was motivation to combine Li and Thaysen, then one of ordinary skill in the art would also substitute the silicon cantilever of Li with the organic, polymer cantilever of Thaysen. In other words, if one of ordinary skill in the art was motivated to combine Li and Thaysen to form a bio-sensor, then the combined bio-sensor would include a cantilever made of the organic polymer of Thaysen. One of ordinary skill in the art would not be motivated to incorporate the bio-sensor feature of Thaysen into the device of Li without also incorporating the polymer material of Thaysen into the device of Li if Thaysen was considered as a whole.

Thus, even if there was motivation to combine Li and Thaysen, the combination would not teach or suggest the inorganic cantilever of claims 43 and 53.

C. Rejections Over Li and Totronese

Claims 40 and 60 are rejected under §103(a) as being unpatentable over Li in view of Tortonese. Applicants respectfully submit that Tortonese does not cure the deficiencies of Li and Thaysen with respect to the amended independent claims 39 and 50. Thus, claims 40 and 60 are believed to be patentable at least for the same reasons as claims 39 and 50.

D. Claims 61-66

Claims 61 and 64 recite measuring the resistance change dynamically over time to detect a dynamic motion of the cantilever as a function of time. In other words, claims 61 and 64 recite a dynamic measurement which measures properties of a vibrating cantilever in response to a biological analyte binding event on the resonator. Claims 62 and 65 recite the use of a resonance frequency of a vibrating cantilever to detect biological analyte binding.

Claims 63 and 66 recite obtaining a frequency spectrum. Li does not teach or suggest these limitations.

In contrast, the detector of Li measures static deflection of the cantilever. The measurement of Li is a static measurement in which an initial reference position of the cantilever is measured and then the deflected position of the resonator is measured. In other words, the detector of Li merely measures the static bending or deflection of the cantilever after the cantilever is pushed down. There is no discussion in Li of mechanical resonance, and what is needed for high-frequency, a.c. mode mechanical operation, including the readout for this regime. Li's frequency discussion merely refers to the readout frequency, i.e. the a.c. bias on the piezoresistor.

Furthermore, the Li paper does not deal with issues involved in displacement transduction for nanoscale mechanical devices which can be used for biological analyte detection. The dimensions really matter in this case because Li's cantilevers are 4 millimeters wide, and the 3 nm, 6 nm and 10 nm thick metal films are not useful for precise measurement in such large scale devices. For example, even for a 100 nm wide piezoresistor, the impedance would probably exceed 100 MegaOhm, which would render it not useful for measurement of the biological analyte at the nanoscale.

As noted in the present specification, one must consider both gauge factor and transducer impedance. This is apparent if one optimizes the output signal to noise ratio at the transducer output. Thus, even though the Li article describes a 30 nm thick Au piezoresistor, it focused on the gauge factor and did not take into account the transducer impedance in order to make useful measurements for the nanoscale devices used to detect biological analyte binding.

III. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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